

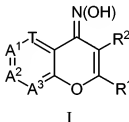
Applicants: Jeremy Green et al.
Application No.: 10/808,678

THE CLAIMS

Please replace all prior versions and listings of claims with the amended claims as follows:

1-46. (Canceled)

47. (Previously presented) A pharmaceutical composition comprising ~~an effective amount of~~ a compound of formula I:



or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle, wherein:

R^1 is Ar^1 or $Cy^1-(L)_mR$, $(L)_mAr^1$, or $(L)_mCy^1$;

R^2 is hydrogen, CN, SR, OR, CO₂R, OC(O)R, C(O)R, C(O)N(R)₂, N(R)₂, or
-N(R)C(O)R;

T is CH [[CR³]];

A¹ is C-halogen, C-CN, or C-R;

each of [[A¹,]] A²[[,]] and A³ is, independently, CR⁴;

R^2 is selected from hydrogen, halogen, NO₂, CN, SR, OR, N(R)₂, or an optionally substituted C₁₋₆ aliphatic group; and

R^4 is selected from halogen, NO₂, CN, $-(L)_mR$, $-(L)_mAr^1$, or $-(L)_mCy^1$; or

two R⁴ groups on adjacent atoms are taken together to form an optionally substituted 5-7 membered partially unsaturated or fully unsaturated ring having 0-3 heteroatoms independently selected from oxygen, sulfur, or nitrogen, wherein[[;]] each ring

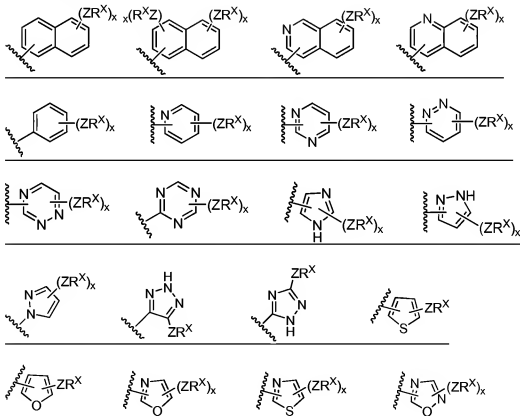
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formed by two R^4 groups on adjacent atoms taken together is optionally substituted with up to 4 occurrences of $Z-R^X$;

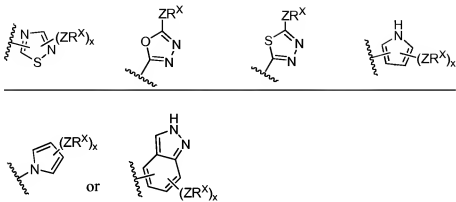
L is $-S-$, $-O-$, $-N(R)-$, or a C_{1-6} alkylidene chain wherein one up to two non adjacent methylene unit[[s]] of L is [[arc]] optionally and independently replaced by $-S-$, $-O-$, $-N(R)-$, $-N(R)C(O)-$, $-N(R)C(S)-$, $-N(R)C(O)N(R)-$, $-N(R)C(S)N(R)-$, $-N(R)CO_2-$, $-C(O)-$, $-CO_2-$, $-C(O)N(R)-$, $-C(S)N(R)-$, $-OC(O)N(R)-$, $-SO_2-$, $-SO_2N(R)-$, or $-N(R)SO_2-[L]-N(R)SO_2N(R)-$, $-C(R)-NN(R)-$, $-C(R)-N-O(R)-$, $-C(O)C(O)-$, or $-C(O)CH_2C(O)-$;

m is 0 or 1;

Ar^1 is selected from

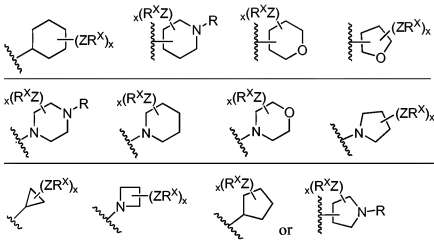


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an optionally-substituted 5-7-membered monocyclic ring or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Cy^1 is selected from



an optionally substituted 3-7 membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered saturated or partially unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein;

Ar¹ and Cy¹ are each optionally substituted with up to 5 occurrences of Z-R^X; wherein

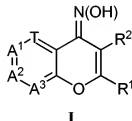
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each occurrence of Z is independently a bond or a C₁₋₆ alkylidene chain, wherein up to two non-adjacent methylene units of Z are optionally replaced by -S-, -O-, -N(R)-, -N(R)C(O)-, -N(R)C(S)-, -N(R)C(O)N(R)-, -N(R)C(S)N(R)-, -N(R)CO₂-, -C(O)-, -CO₂-, -C(O)N(R)-, -C(S)N(R)-, -OC(O)N(R)-, -SO₂-, -SO₂N(R)-, or -N(R)SO₂-[[,]] -N(R)SO₂N(R)-, -C(R)=NN(R)-, -C(R)=N O(R)-, -C(O)C(O)-, or -C(O)CH₂C(O)-; each occurrence of R^X is independently selected from -R', halogen, NO₂, CN, -OR', -SR', or -N(R')₂, -N(R')C(O)R', -N(R')C(S)R', -N(R')C(O)N(R')₂₅, -N(R')C(S)N(R')₂₅, -N(R')CO₂R', -C(O)R', -C(S)R', -CO₂R', -OC(O)R', -C(O)N(R')₂₅, -C(S)N(R')₂₅, -OC(O)N(R')₂₅, -S(O)R', -SO₂R', -S(O)₂R', -SO₂N(R')₂₅, -N(R')SO₂R', -N(R')SO₂N(R')₂₅, -C(O)C(O)R', -C(O)CH₂C(O)R', -NR'NR'C(O)R', -NR'NR'C(O)N(R')₂₅, -NR'NR'CO₂R', -C(O)N(OR')R', -C(NOR')R', -S(O)₂R', -N(OR')R', -C(=NH)N(R')₂₅; or -(CH₂)₀₋₂₅NHC(O)R'; wherein each occurrence of R is independently hydrogen or ~~a~~ an optionally substituted C₁₋₆ aliphatic group[[,]]; and each occurrence of R' is independently hydrogen, ~~[[or]]~~ ~~a~~ an optionally substituted C₁₋₆ aliphatic group, ~~a~~ an optionally substituted C₆₋₁₀ aryl ring, ~~a~~ an optionally substituted heteroaryl ring having 5-10 ring atoms, or ~~a~~ an optionally substituted heterocycl ring having 3-10 ring atoms; or R and R' or two occurrences of either R or R' are taken together with the atoms to which they are bound to form an optionally substituted 5-8 membered saturated, partially unsaturated, or aryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or two occurrences of either R' or R on the same nitrogen are taken together with the nitrogen atom to which they are bound to form an optionally substituted 5-8 membered saturated, partially unsaturated, or aryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

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48-49. (Canceled)

50. (Currently amended) A method of inhibiting c-MET kinase activity in a biological sample, wherein said biological sample is selected from a cell culture, biopsied material obtained from a mammal, saliva, urine, feces, semen, or tears, or an extract thereof; which method comprises contacting said biological sample with a composition according to claim 47 or a compound of formula I:



or a pharmaceutically acceptable salt thereof, wherein:

R^1 is Ar^1 or $Cy^1-(L)_mR$, $(L)_mAr^1$, or $(L)_mCy^1$;

R^2 is hydrogen, CN, SR, OR, CO₂R, OC(O)R, C(O)N(R)₂, N(R)₂, or N(R)C(O)R;

T is CH [[CR³]];

A^1 is C-halogen, C-CN, or C-R;

each of [[A¹,]] A²[[,]] and A³ is, independently, CR⁴;

R^3 is selected from hydrogen, halogen, NO₂, CN, SR, OR, N(R)₂, or an optionally substituted C₁₋₆ aliphatic group; and

R^4 is selected from halogen, NO₂, CN, -(L)_mR, -(L)_mAr¹, or -(L)_mCy¹; or

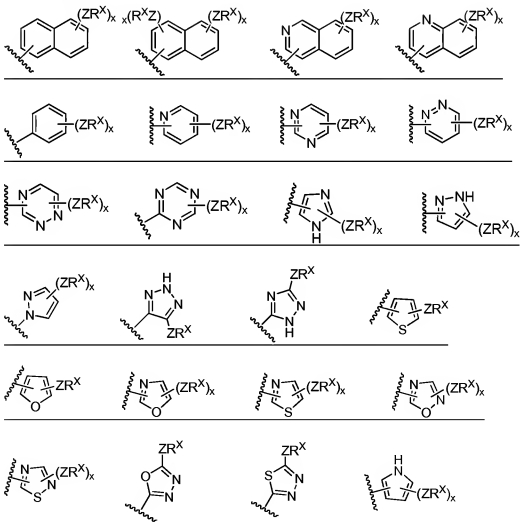
two R⁴ groups on adjacent atoms are taken together to form an optionally substituted 5-7 membered partially unsaturated or fully unsaturated ring having 0-3 heteroatoms independently selected from oxygen, sulfur, or nitrogen, wherein[[;]] each ring formed by two R⁴ groups on adjacent atoms taken together is optionally substituted with up to 4 occurrences of Z-R^x;

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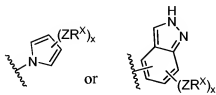
L is ~~S~~, ~~O~~, ~~N(R)~~, or a C₁₋₆ alkylidene chain wherein one up to two non-adjacent methylene unit[[s]] of L is [[arc]] optionally and independently replaced by ~~S~~, ~~O~~, ~~N(R)~~, ~~N(R)C(O)~~, ~~N(R)C(S)~~, ~~N(R)C(O)N(R)~~, ~~N(R)C(S)N(R)~~, ~~N(R)CO₂~~, ~~C(O)~~, ~~CO₂~~, ~~C(O)N(R)~~, ~~C(S)N(R)~~, ~~OC(O)N(R)~~, ~~SO₂~~, ~~SO₂N(R)~~, or ~~N(R)SO₂~~[[.]] ~~N(R)SO₂N(R)~~, ~~C(R)=NN(R)~~, ~~C(R)=N-O(R)~~, ~~C(O)C(O)~~, or ~~C(O)CH₂C(O)~~;

m is 0 or 1;

Ar¹ is selected from

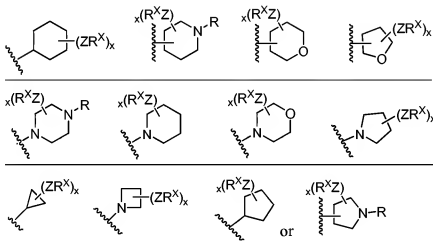


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an optionally-substituted 5-7 membered monocyclic ring or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Cy¹ is selected from



an optionally-substituted 3-7 membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or an 8-10 membered saturated or partially unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein;

Ar¹ and Cy¹ are each optionally substituted with up to 5 occurrences of Z-R^X; wherein each occurrence of Z is independently a bond or a C₁₋₆ alkylidene chain, wherein up to two non-adjacent methylene units of Z are optionally replaced by -S-, -O-, -N(R)-, -N(R)C(O)-, -N(R)C(S)-, -N(R)C(O)N(R)-, -N(R)C(S)N(R)-, -N(R)CO₂-, -C(O)-, -CO₂-, -C(O)N(R)-, -C(S)N(R)-, -OC(O)N(R)-, -SO₂-, -SO₂N(R)-, or -N(R)SO₂[[,]] -N(R)SO₂N(R)-, -C(R)-NN(R)-, -C(R)-N O(R)-, -C(O)C(O)-, or -C(O)CH₂C(O)-;

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each occurrence of R^X is independently selected from $-R'$, halogen, NO_2 , CN , $-OR'$, $-SR'$, or $-N(R')_2$, $-N(R')C(O)R'$, $-N(R')C(S)R'$, $-N(R')C(O)N(R')_{25}$, $-N(R')C(S)N(R')_{25}$, $-N(R')CO_2R'$, $-C(O)R'$, $-C(S)R'$, $-CO_2R'$, $-OC(O)R'$, $-C(O)N(R')_{25}$, $-C(S)N(R')_{25}$, $-OC(O)N(R')_{25}$, $-S(O)R'$, $-SO_2R'$, $-S(O)_2R'$, $-SO_2N(R')_{25}$, $-N(R')SO_2R'$, $-N(R')SO_2N(R')_{25}$, $-C(O)C(O)R'$, $-C(O)CH_2C(O)R'$, $-NR'NR'C(O)R'$, $-NR'NR'C(O)N(R')_{25}$, $-NR'NR'CO_2R'$, $-C(O)N(OR')R'$, $-C(NOR')R'$, $-S(O)_2R'$, $-N(OR')R'$, $-C(=NH)N(R')_{25}$ or $-(CH_2)_{0-2}NHC(O)R'$; wherein

each occurrence of R is independently hydrogen or a ~~an optionally substituted~~ C_{1-6} aliphatic group[,], and

each occurrence of R' is independently hydrogen, [[or]] ~~a~~ ~~an optionally substituted~~ C_{1-6} aliphatic group, a ~~an optionally substituted~~ C_{6-10} aryl ring, a ~~an optionally substituted~~ heteroaryl ring having 5-10 ring atoms, or a ~~an optionally substituted~~ heterocycl ring having 3-10 ring atoms; or

R and R' or two occurrences of either R or R' are taken together with the atoms to which they are bound to form an optionally substituted 5-8 membered saturated, partially unsaturated, or aryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or

two occurrences of either R' or R on the same nitrogen are taken together with the nitrogen atom to which they are bound to form an optionally substituted 5-8 membered saturated, partially unsaturated, or aryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur..

51. (Canceled)

52. (Withdrawn) A method of treating or lessening the severity of a disease or condition in a patient selected from gastric cancer, pancreatic cancer, ovarian cancer,

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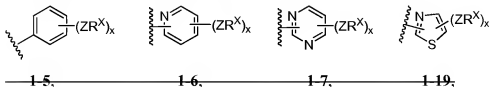
breast cancer, or prostate cancer comprising the step of administering to said patient a composition of claim 47.

53. (Withdrawn) The method according to claim 52, comprising the additional step of administering to said patient an additional therapeutic agent selected from mechlorethamine, chlorambucil, cyclophosphamide, melphalan, ifosfamide, methotrexate, 6-mercaptopurine, 5-fluorouracil, cytarabine, gemcitabine, vinblastine, vincristine, vinorelbine, paclitaxel, etoposide, irinotecan, topotecan, doxorubicin, bleomycin, mitomycin, carmustine, lomustine, cisplatin, carboplatin, asparaginase, and tamoxifen, leuprolide, flutamide, megestrol, imatinib (Gleevec™), adriamycin, dexamethasone, or cyclophosphamide, wherein:

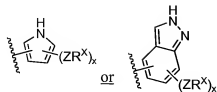
said additional therapeutic agent is appropriate for the disease being treated; and
said additional therapeutic agent is administered together with said composition as a single dosage form or separately from said composition as part of a multiple dosage form.

54-59. (Canceled)

60. (Currently amended) The composition according to claim 47 [[59]], wherein Ar¹ is selected from one of the following groups:



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— **1-24,** — **or 1-26,**

wherein x is 0-5.

61-80. (Canceled)

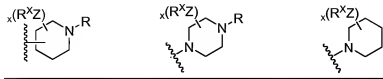
81. (Previously presented) The composition according to claim 47, wherein A^2 is CR^4 and R^4 is halogen, CN, $-(L)_mR$, $-(L)_mAr^1$, or $-(L)_mCy^1$.

82. (Canceled)

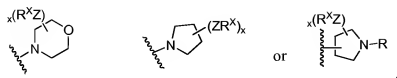
83. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 and R^4 is halogen or R.

84. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 and R^4 is $-(L)_mR$, wherein L is -O- or -N(R)-.

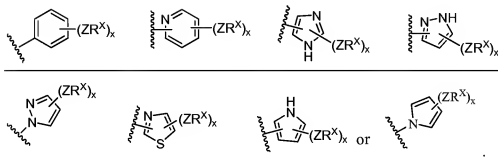
85. (Currently amended) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mCy^1$, m is 0 and Cy^1 is **2-2, 2-5, 2-6, 2-7, 2-8, or 2-12**



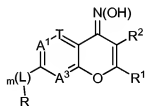
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86. (Currently amended) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mAr^1$, m is 0 and Ar^1 is **1-5, 1-6, 1-11, 1-12, 1-13, 1-19, 1-24, or 1-25**



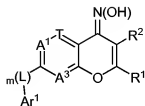
87. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mR$, and compounds have the formula **IE-1**:



IE-1.

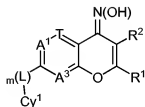
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88. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mAr^1$, and compounds have the formula **IE-2**:



IE-2 .

89. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mCy^1$, and compounds have the formula **IE-3**:



IE-3 .

90. (Previously presented) The composition according to claim 47, wherein A^3 is CR^4 and R^4 is halogen, CN, $-(L)_mR$, $-(L)_mAr^1$, or $-(L)_mCy^1$.

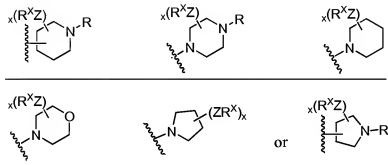
91. (Canceled)

92. (Previously presented) The composition according to claim 90, wherein A^3 is CR^4 and R^4 is halogen or R.

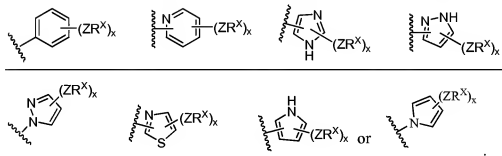
93. (Previously presented) The composition according to claim 90, wherein A^3 is CR^4 and R^4 is $-(L)_mR$, wherein L is $-O-$ or $-N(R)-$.

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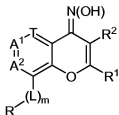
94. (Currently amended) The composition according to claim 90, A^3 is CR^4 , R^4 is $-(L)_mCy^1$, m is 0 and Cy^1 is **2-2**, **2-5**, **2-6**, **2-7**, **2-8**, or **2-12**



95. (Currently amended) The composition according to claim 90, wherein A^3 is CR^4 , R^4 is $-(L)_mAr^1$, m is 0 and Ar^1 is **1-5**, **1-6**, **1-11**, **1-12**, **1-13**, **1-19**, **1-24**, or **1-25**



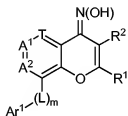
96. (Previously presented) The composition according to claim 90, wherein A^3 is CR^4 , R^4 is $-(L)_mR$, and compounds have the formula **IF-1**:



IF-1 .

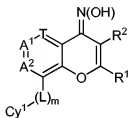
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97. (Previously presented) The composition according to claim 90, wherein A^3 is CR^4 , R^4 is $-(L)_mAr^1$, and compounds have the formula **IF-2**:



IF-2 .

98. (Previously presented) The composition according to claim 90, wherein A^3 is CR^4 , R^4 is $-(L)_mCy^1$, and compounds have the formula **IF-3**:

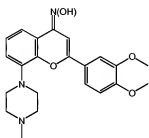


IF-3 .

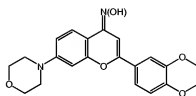
99-100. (Canceled)

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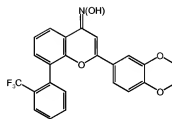
101. (Currently amended) The composition according to claim 47, selected from one of the following compounds:



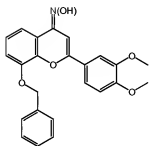
I-1,



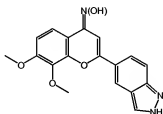
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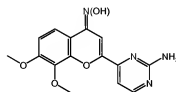
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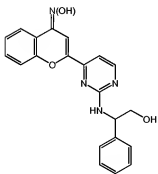
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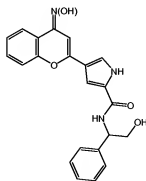
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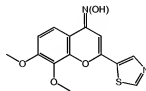
I-6,



I-7,

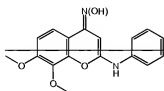


I-8,

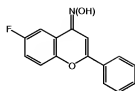


I-9,

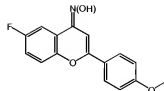
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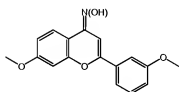
[[I-10,]]



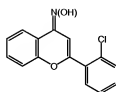
I-11,



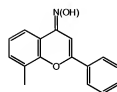
I-12,



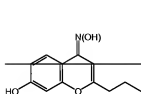
I-13,



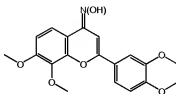
I-14,



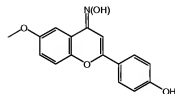
I-15,



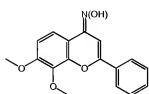
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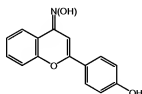
I-17,



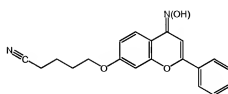
I-18,



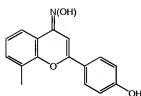
I-19,



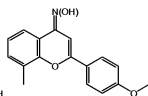
I-20,



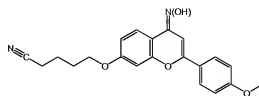
I-21,



I-22,

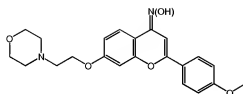


I-23,

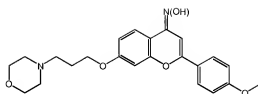


I-24,

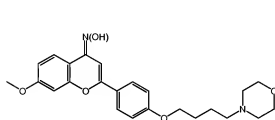
Applicants: Jeremy Green et al.
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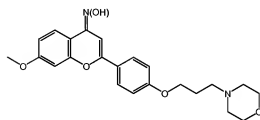
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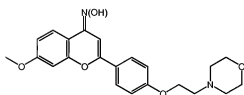
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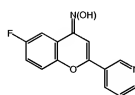
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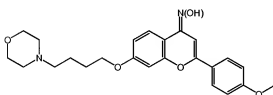
I-28,



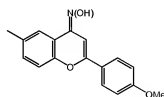
I-29,



I-30,

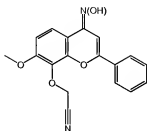


I-31,

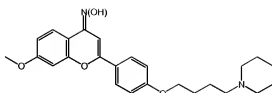


I-32,

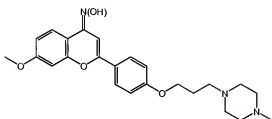
Applicants: Jeremy Green et al.
Application No.: 10/808,678



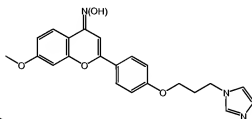
I-33,



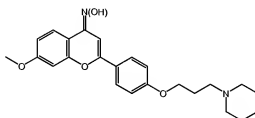
I-34,



I-35,



I-36,



or I-37 .